Introduction

Generic drugs are reproductions of the original innovator medicine which are made widely available when a drug's patent expires. They have been widely used in many countries for over 40 years, including New Zealand. The use of generic medicines is an important part of health care, providing economical alternatives to more expensive branded products and allowing considerable savings for the overall health care budget. With this potential for savings the use of quality generic medicines is becoming increasingly part of national medicines management strategies. For example, the UK will introduce generic substitution from 2010 and there are similar initiatives in Australia.

We can expect the use of generic medicines to increase in New Zealand. This publication is intended to inform health professionals about the processes by which generic medicines are tested, approved and monitored, to provide reassurance of their quality, safety and effectiveness. As our patients are often misinformed or have concerns about the use of generic medicines we also provide advice on how to increase acceptance of generics amongst patients. Finally, we discuss the monitoring processes in place in New Zealand to ensure that if problems do occur they are identified and resolved in a timely manner.

A few words about the terminology used in this publication. When we mention brand switching it will usually mean a switch from an innovator brand such as the Aropax brand of paroxetine to Loxamine, which is the generic brand. Occasionally, the generic medicine does not have a brand name and may be simply known by the approved chemical name. When bioequivalence studies are described, we refer to the generic compared to the innovator medicine.

What is **Bioavailability** and **Bioequivalence?**

All generic medicines in New Zealand are approved by Medsafe and have been shown to be bioequivalent to innovator medicines, according to internationally accepted criteria and standards.[1] This means that any differences in bioavailability between generic and innovator medicines are not clinically significant.

Bioavailability

Bioavailability is a measurement of the extent of a therapeutically active medicine that reaches the systemic circulation and is therefore available at the site of action.

For most medicines that are taken orally, the active ingredients are released in the gastrointestinal (GI) tract and arrive at their site of action via the systemic circulation. Blood concentrations of the active ingredients and/or their active metabolites thereby provide a marker for the concentration at the site of action and a valid measure of bioavailability.

A blood concentration – time curve (achieved by serial measurements over time) reflects not just the release of the active ingredient from the medicine and its absorption from the GI tract, but also other factors including pre-systemic metabolism, distribution and elimination.

Bioavailability is assessed using three main pharmacokinetic variables (see Figure 1);

- the area under the blood drug concentration versus time curve (AUC)
- the maximum blood concentration (C_{max})
- the time to reach maximum concentration (T_{max})

Bioavailability example

A hypothetical drug given orally has a bioavailability of 50% (or 0.5), this is due to:

1. incomplete absorption in the GI tract so that only 70% of the initial dose is absorbed.
2. subsequent metabolism of a further 20% before it reaches the systemic circulation (e.g. first pass through the liver).

Therefore only 50% of the original oral dose reaches the systemic circulation.